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FORMATION OF ECTOPIC OSTEOGENESIS IN WEIGHTLESSNESS

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16. Abstract An ectopic osteogenesis experiment aboard the Cosmos-936 biosatellite, with its synchronous ground test and vivarium controls, is described. Decalcified, lyophilized femur and tibia were implanted under the fascia or in the anterior wall of the abdomen. Bone formation before and after the tests is described and illustrated. The extent of formation of ectopic bone in weightlessness does not differ signi- ficantly from that in the ground controls, but the bone marrow of the ectopic bone of the flight rats consisted exclusively of fat cells. The deficit of support-muscle loading is considered to cause the disturbance in skeletal bone tissue development.			
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FORMATION OF ECTOPIC OSTEOGENESIS IN WEIGHTLESSNESS

Steady attention is being given to the effect of space flight factors on skeletal bony tissue. It is well known that, in weightlessness, deterioration of the bone formation process (osteoporosis) and loss of Ca occur. Disorders in skeletal tissue can be considered as a "weightlessness barrier" (in the descriptive expression of Hatner and McMillan, 1968), which can significantly limit the duration of space flights. Similar changes in bony tissue are observed in hypokinesia. The common character of development of the nature of the changes of bony tissue in weightlessness and in hypokinesia gives a basis for proposing that bone formation disorders are the result of a deficit of the support-muscle load. However, it need not be thought that the lack of mechanical loading can be the only cause of osteogenesis disorders. It is not excluded that disruption of the bone formation process in space flight may be connected with change in the system (neurohormonal), which regulates the formation and remodelling of bone.

To test the propositions expressed, it is advisable to induce the development of bone outside the skeleton (ectopically), i.e., in places where bony tissue does not develop, either ontogenetically or phylogenetically. A convenient model of ectopic osteogenesis is the implantation of a decalcified, lyophilized bony matrix which secretes the osteogenesis inducer during its resorption, in the anterior wall of the abdomen (Urist, 1965-1970). It is significant that ectopic bone has all the morphological and histochemical characteristics of skeletal bony tissue.

Material and Methods

Preparation of the bony matrix and preservation of its

* Numbers in the margin indicate pagination in the foreign text.

inducing capacity were carried out by the method described by Urist (1965-1974). SPF line rats were used in the tests. A decalcified, lyophilized bony matrix of the femur and tibia was implanted in them, under the fascia or in the anterior wall of the abdomen. Three groups were made up from the test rats: flight group (10 rats); synchronous ground test (10 rats); and vivarium control group (7 rats). A portion of the animals (5 rats each) from the flight group and synchronous test were killed on the day the test was conducted, and the remaining animals, immediately after the end of the test. On day 10-13 after implantation of the matrix, the animals of all groups were immunized with sheep erythrocytes. All animals were maintained on a "space diet" before and after implantation. /2

Test results

In the animals killed on the biosatellite launch day (22 days after matrix implantation) or on the day of conduct of the synchronous ground test (19 days after implantation), upon visual inspection, the bony matrix was hard. This indicates the deposition of Ca salts. Upon microscopic analysis, individual sections of new, coarse fibered bone were found, the development of which was observed, both at points of resorption of the cortical part of the matrix, and inside the cavity, as viewed from the endosteum of the old bone (Figs. 1, 2). In the bone marrow cavity of the old bone, as a rule, coarse fibered, combined with delicate fibered connective tissue developed, permeated by small vessels. In the cortical section of the matrix, resorption was intensive, owing to the presence of multinucleate symplasts, similar to osteoclasts in morphology. Thus, before the start of the test, the development of ectopic bone in all rats indicates the capacity of the bony matrix to induce new bone.

After the end of the test, further development of ectopic

bone prevailed in all rats (Fig. 3), the volume of which was somewhat larger than in the "prelaunch period." It is significant that no important differences were found in the amount of new bone, between the rats from the flight group (40 days after implantation of the bony matrix), the synchronous ground test (38 days after implantation) and the vivarium control (48 days after implantation). However, the periods of development of the new bone (approximately 6-7 weeks), for example, in the control rats, permitted considerably active bone formation to be hoped for, since preliminary tests showed that, in the period of 6-7 weeks after implantation, the amount of ectopic bone in the intact animals (the rats of this group were maintained in vivaria on the normal diet) reached greater amounts than in the test rats (Figs. 4,5). Since the test rats were immunized 13 and maintained on the "space diet" beforehand, this gives a basis for assuming that these differences were due to these factors. The latter possibly slow down, but do not stop growth of ectopic bone in all the test animals. The development of bony tissue, against a background of activation of T-system immunity or as a result of the "space diet," is not known. At the same time, there are data, which indirectly indicate connections between immune system activity and the growth rate of bony tissue (Mandi, 1975; Laitinen, 1976; Reddi, 1976).

In space flight, just as in the control, resorption of the old matrix was just as active as in the preflight period. In distinction from the preflight condition bony and cartilaginous tissue developed during the flight. The vigorous growth of coarse fibered connective tissue and focal, sometimes extensive hemorrhages in it in the marrow cavity of the old bone should also be noted. At the location of the cortical bone of the matrix, frequently in its cavity, together with the development of new bone, bone marrow develops. The cellular nature of the ectopic bone marrow of the flight group rats was

less pronounced than the cellular nature of the control rat bone marrow.

Thus, the test results showed that the degree of development of ectopic bone in weightlessness does not differ significantly from that of the control group rats. At the same time, distinct differences were found in the cellular nature of the bone marrow. The marrow which developed in the zone of ectopic bone of the flight rats consisted exclusively of fat cells. This pattern is similar to bone marrow aplasia, after exposure to large radiation doses, which cause the bone marrow syndrome.

In summarizing the results of the studies, a preliminary conclusion can be drawn that the development of bone outside the skeleton is not subject to the effect of space flight factors. This enables it to be considered that disorders in the development of skeletal bony tissue which occur in weightlessness are, rather, connected with the deficit in support muscle loading, than with change in neurohormonal regulation of the bone formation process.

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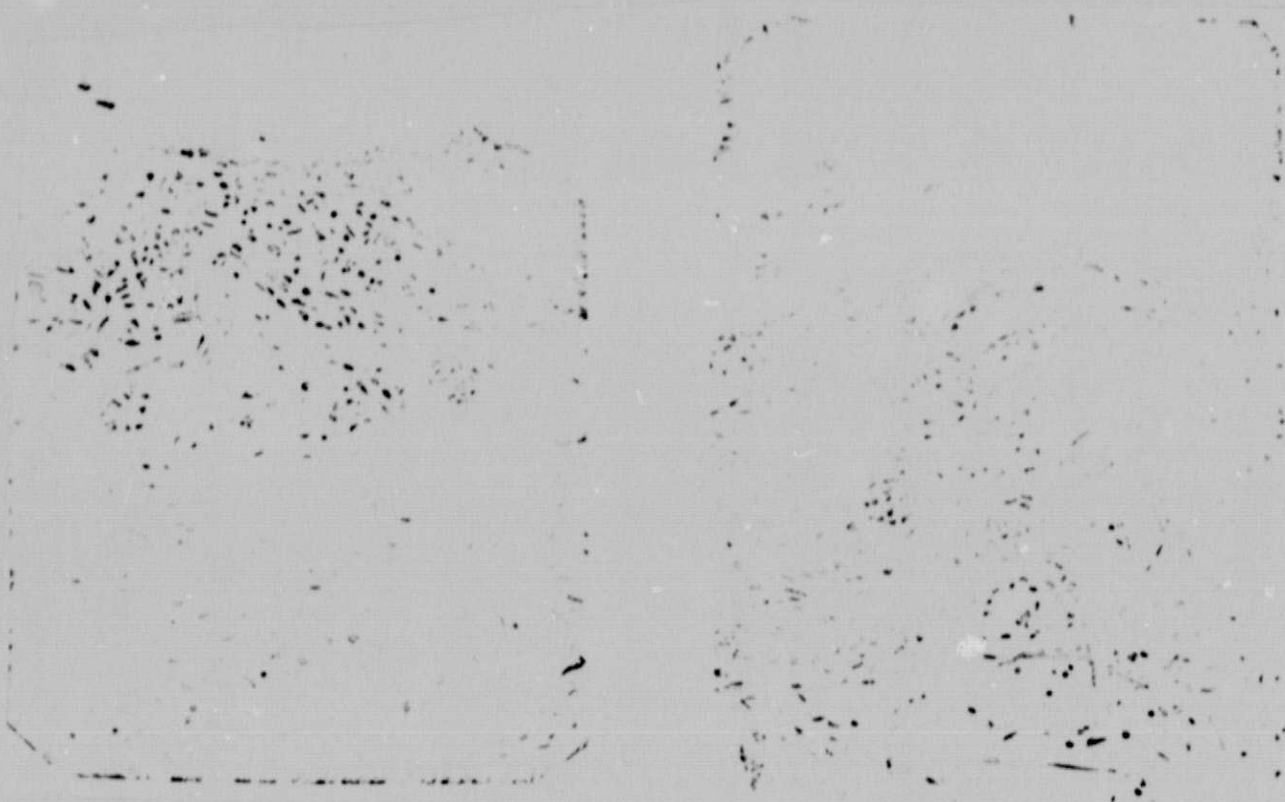


Fig. 1. Development of ectopic bone in rats killed on launch day of Cosmos-936 biosatellite; 22 days after matrix implantation; magnification, objective 20, eyepiece 6.

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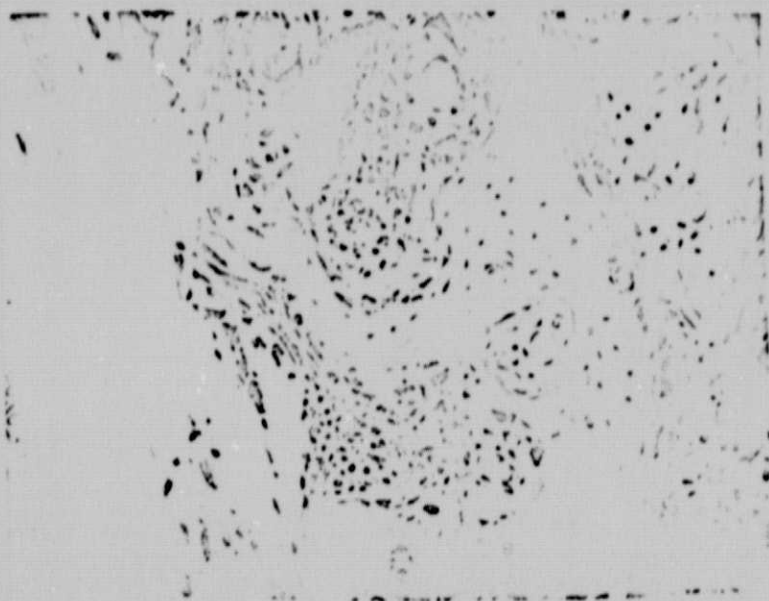


Fig. 2. Development of ectopic bone in rats killed on day of synchronous ground test; 19 days after matrix implantation; magnification, objective 20, eyepiece 6.

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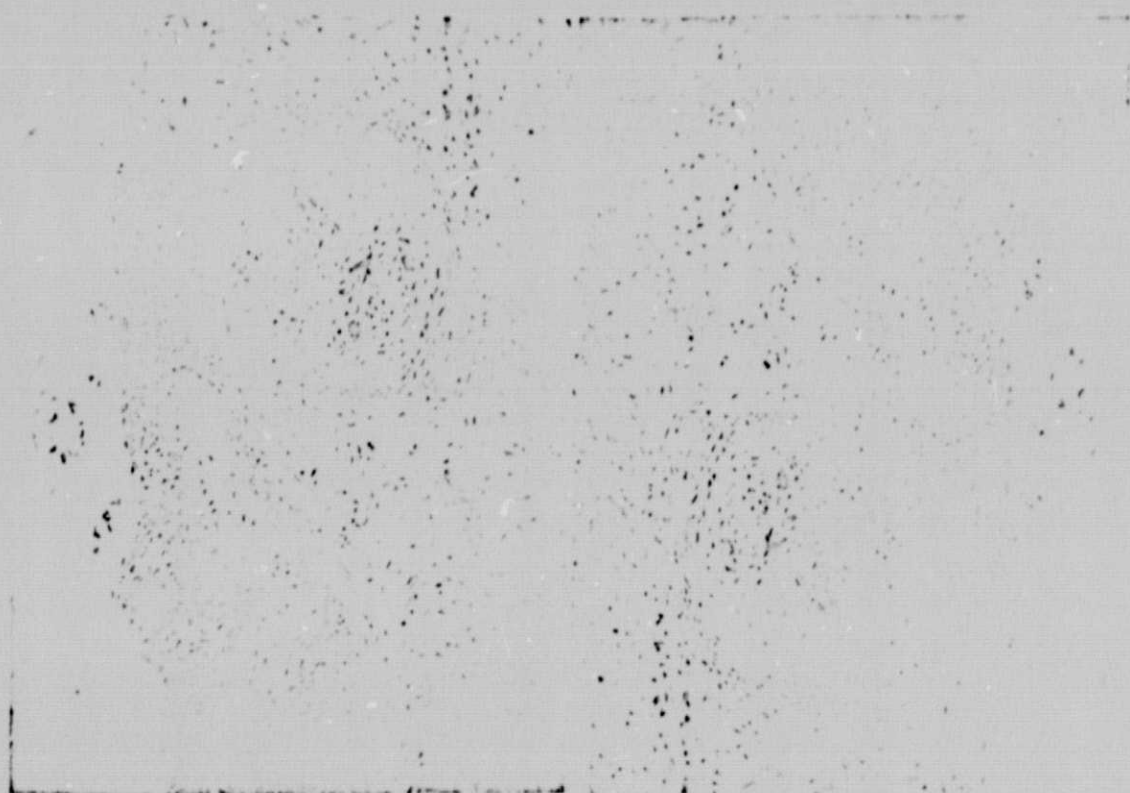


Fig. 3. Development of ectopic bone in rats killed on day of end of space flight; 40 days after matrix implantation; magnification, objective 10, eyepiece 6.

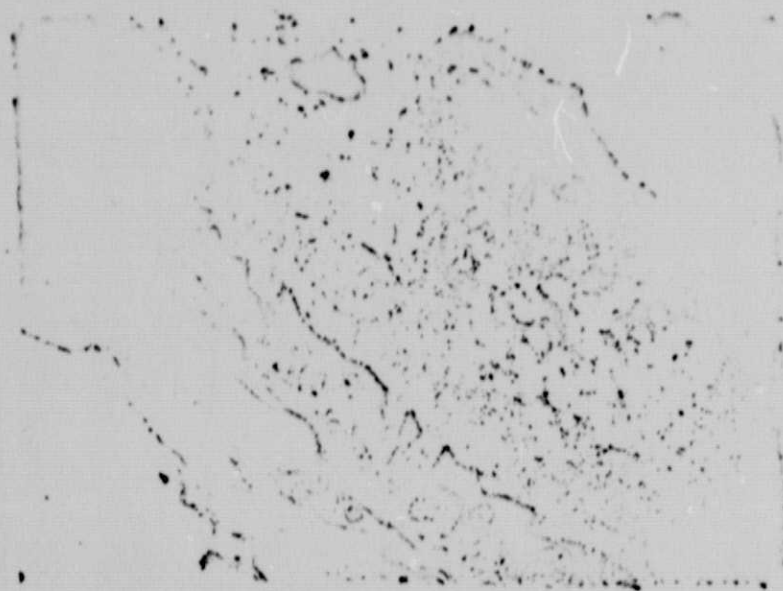


Fig. 4. Mature, newly formed bone tissue with bone marrow; 7 weeks after implantation; magnification, objective 10, eyepiece 6.

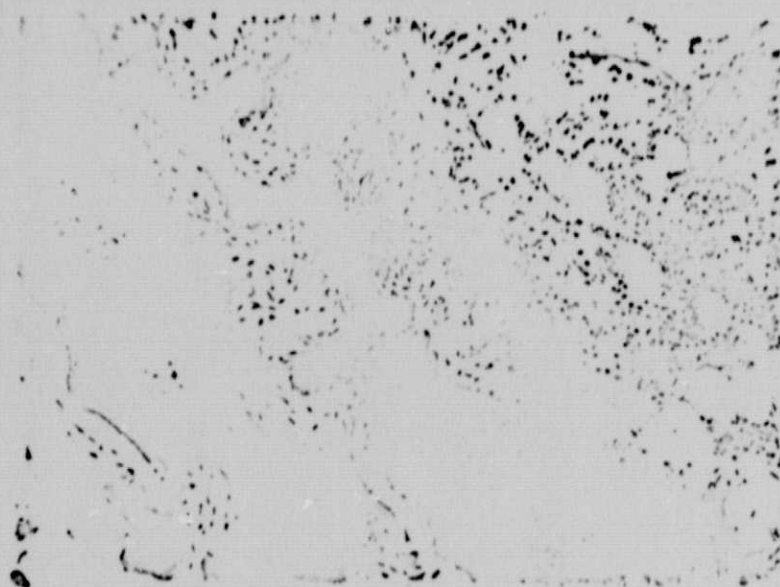


Fig. 5. Thin, amorphous substance is noted between newly formed bone tissue and bone marrow; apparently future prototype of endosteum; 7 weeks after implantation; magnification, objective 20, eyepiece 6.

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